UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/615,615	07/08/2003	Clemens Hendricus, M. Kocken	2183-6041US	8276

24247 7590 04/01/2009

TRASKBRITT, P.C.
P.O. BOX 2550
SALT LAKE CTTY, UT 84110

EXAMINER	
HIBBERT, CATHERINE S	

ART UNIT	PAPER NUMBER
1636	

NOTIFICATION DATE	DELIVERY MODE
04/01/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

USPTOMail@traskbritt.com

Office Action Summary	Application No.	Applicant(s)	
	10/615,655	KOCKEN ET AL.	
	Examiner	Art Unit	
	CATHERINE S. HIBBERT	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,8-10,27-30 and 46-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 8-10, 27-30, and 46-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3 July 2008 has been entered.

Applicant's Amendments to the Claims, filed 3 July 2008, have been received and entered. Claims 5-7, 11-26 and 31-45 are cancelled. Claim 48 is new. Claims 1-4, 8-10, 27-30, and 46-48 are pending and under consideration in this action.

Sequence Listing Rules Compliance

Figure 1 discloses **an amino acid** sequence that is not properly identified with a sequence identifier (i.e. "SEQ ID NO:"). Sequence Listing, See 37 CFR 1.821-1.825 and MPEP §§ 2421-2431. In addition, additional amino acid sequences are disclosed in the specification (e.g. page 6, lines 6-7). The requirement for a sequence listing applies to all sequences disclosed in a given application, whether the sequences are claimed or not. See MPEP § 2421.02. If said sequences were originally submitted in both electronic and paper format, then applicant is only required to make proper amendment to the Brief Description of the Drawings (i.e. with proper sequence identifiers). However,

if applicant has not previously submitted said sequences, then a new submission is also required (i.e. CD-ROM/CD-R, Paper Copy and Attorney Declaration).

Claim Objections

Objections made in the prior Office Action to Claims 1, 27, 46 and 47 are withdrawn herein based on Applicant's Amendments to the Claims filed 3 July 2008.

Claim 47 is newly objected to because the phrase "an amino acid sequence residues" in lines 6-7 contains a typographical/grammatical error. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 27, and 46-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, and therefore also dependent Claims 2-4 and 8-10, are indefinite because Claim 1 recites "an amino acid sequence selected from the group consisting of 25-442, 97-442, and 97-545 of SEQ ID NO:6" (lines 5-7) however SEQ ID NO:6 refers to a polynucleotide sequence rather than to an amino acid sequence. As noted above, Figure 1 is lacking sequence identifiers for the amino acid sequences that correspond to the nucleic acid sequence of SEQ ID NO:6.

Claim 27, and therefore also dependent Claims 28-30, are indefinite because Claim 27 recites "an amino acid sequence selected from the group consisting of 25-442, 97-442, and 97-545 of SEQ ID NO:6" (lines 6-8) however SEQ ID NO:6 refers to a polynucleotide sequence rather than to an amino acid sequence.

Claim 46, 47 and 48 are indefinite because the claims recite "an amino acid sequence selected from the group consisting of 25-442, 97-442, and 97-545 of SEQ ID NO:6" (lines 5-8) however SEQ ID NO:6 refers to a polynucleotide sequence rather than to an amino acid sequence.

Additionally, Claims 1, 46 and 48 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: Claims 1, 46 and 48 are directed to a method for producing mRNA comprising a step of providing a yeast cell with a nucleic acid encoding a polypeptide, but are lacking a step of expressing the nucleic acid in the cell in order to make the mRNA.

Additionally, Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: expressing an mRNA into a polypeptide, as an essential step before "purifying" the polypeptide.

Additionally, Claims 27 and 47 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: expressing an mRNA into a polypeptide, as an essential step before "collecting" the formed polypeptide.

Additionally, Claim 47 recites the limitation "the fragment thereof of FIG 1" in lines 9-10. There is insufficient antecedent basis for this limitation in the claim because a fragment of FIG. 1 has not been previously mentioned in the claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 8-10, 27-30, 46 and 47 STAND rejected and new Claim 48 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for reasons of record and presented herein. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicants arguments have been fully considered but are respectfully not found persuasive because the MPEP states that the purpose of the written description

requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966." *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not a sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if

the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include: (1) Actual reduction to practice, (2) Disclosure of drawings or structural chemical formulas, (3) Sufficient relevant identifying characteristics (such as: i. Complete structure, ii. Partial structure, iii. Physical and/or chemical properties, iv. Functional characteristics when coupled with a known or disclosed, and correlation between function and structure), (4) Method of making the claimed invention, (5) Level of skill and knowledge in the art, and (6) Predictability in the art.

Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

Initially, it is noted that Applicants do provide written description for:

a method for producing mRNA encoding a *Plasmodium falciparum* apical membrane antigen-1 (AMA-1) ectodomain, or a fragment thereof, in a yeast cell, said method comprising: providing said yeast cell with an expression vector comprising the nucleic acid sequence consisting of SEQ ID NO:6, and for:

a method for producing mRNA encoding a *Plasmodium falciparum* apical membrane antigen-1 (AMA-1) ectodomain, or a fragment thereof, in a yeast cell, said method comprising: providing said yeast cell with an expression vector comprising the nucleic acid sequence consisting of the polynucleotide fragments of the sequence SEQ ID NO:6 that encode the amino acid sequences 25-442, 97-442, and 97-545 shown in Figure 1.

However, the claims lack written description for that which encompasses critical sequences that are not known but which require experimentation to obtain, particularly due to the unpredictable nature of Applicants invention. For example, because the *Plasmodium falciparum* AMA-1 ectodomains and fragments are not necessarily interchangeable, there can be Plasmodium variant-, strain-specific or even host specific immunity indicating Variant- and Strain-specific immunity in a simian species infected with *Plasmodium Falciparum* (e.g., Fandeur et al. Am. J. Trop. Med. 1998; 58(2): 225-31; e.g. abstract; of record). Therefore, even amongst a small number of embodiments of Plasmodium falciparum AMA- 1 ectodomains claimed for which the explicit critical sequence is unknown and would require experimentation to obtain, a functional correlation between such a sequence efficiently producing a properly folded protein of interest is lacking.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the *entire scope* of the claimed invention.

Applicants response is to traverse the rejection by amendment and argument stating "the Specification provides more than adequate written description of the *Plasmodium falciparum* AMA-1 ectodomain fragments, as presently claimed". Additionally, Applicant submit that the skill and knowledge concerning nucleotides sequences in the biotechnological arts is very high and thus the representative number of species provided by actual reduction to practice in order to provide sufficient written description of the genus of "variants" is lessened. Additionally, Applicants argue that:

> As currently amended, claims 1, 27, 46, and 47 recite, in part, providing a yeast cell with an isolated or recombinant nucleic acid encoding Plasmodium f. ectodomain or a fragment thereof. The claims further define the encoding nucleic acid and/or fragments thereof in accordance with the subject matter described in the Specification (e.g., "wherein the encoding nucleic acid comprises the nucleotide sequence of FIG. 1" and "wherein the fragment thereof comprises an amino acid sequence selected from the group consisting of 25-442, 97-442, and 97- 545 of SEQ ID NO: 6").

In addition, Applicants state that:

> each of claims 1, 27, 46, and 47 has been amended substituting "functional part" with "fragment," or "fragment thereof," in addition to deleting "corresponding to." Additionally, the amended claims further clarify "fragment," or "fragment thereof" as comprising an amino acid sequence selected from the group consisting of 25-442, 97-442, and 97-545 of SEQ ID NO: 6. Applicants submit that the claimed fragments are more than adequately described in the Specification.

Furthermore, Applicants disagrees that the term "comprises a nucleotide sequence of FIG. 1" reads on any consecutive sequences of at least two nucleotides. Applicants note that the pertinent language of the *presently amended* claim 1 recites "comprises a nucleotide sequence of FIG. 1 encoding the ectodomain or the fragment thereof." Applicants further state that "The claim further identifies the fragments thereof as amino acid sequences 25-442, 97-442, and 97-545" and conclude "Thus, the claim is not directed to any nucleotide sequence of FIG. 1, but rather those nucleotide sequences that encode the ectodomain and fragments thereof". In addition, Applicant notes that claims have been amended to recite "wherein at least one glycosylation site is removed from said Plasmodium falciparum AMA-1 ectodomain or said fragment thereof" and argue, therefore, that "the claims, as presently amended, are directed to subject matter described in the Specification". In addition, Applicants submit that the Examiner's remarks with regard to claim 8 are now moot in light of the amendments to the base claim 1 and Applicants remarks above. In conclusion, Applicants submit that the presently amended claims are supported by the Specification and meet the written description requirement.

Applicants arguments have been fully considered but are respectfully not found persuasive. Specifically, while Applicants provide written description for: a method for

producing mRNA encoding a *Plasmodium falciparum* apical membrane antigen-1 (AMA-1) ectodomain, or a fragment thereof, in a yeast cell, said method comprising: providing said yeast cell with an expression vector comprising the nucleic acid sequence consisting of SEQ ID NO:6, and for a method for producing mRNA encoding a *Plasmodium falciparum* apical membrane antigen-1 (AMA-1) ectodomain, or a fragment thereof, in a yeast cell, said method comprising: providing said yeast cell with an expression vector comprising the nucleic acid sequence consisting of the polynucleotide fragments of the sequence SEQ ID NO:6 that encode the amino acid sequences 25-442, 97-442, and 97-545 shown in Figure 1, the amended claims, as written, read broadly on methods using nucleic acid sequences that have been further limited with unspecified modifications to the nucleotide/amino acid sequences and require functional limitations to these myriad of potentially modified sequences. As such, since the nature of the functional requirements for the constructs is a critical element to the invention (i.e. producing properly folded proteins that are recognized by specific antibodies for vaccine production) and because the state of the art teaches that the precise sequences used are critical towards that end and would require experimentation to determine which sequences could be used in Applicants invention, it is concluded that Applicants were not in possession of the full breadth of Applicants claims at the time of Applicants invention.

State of the Prior Art

At the time of Applicants invention, it was known in the art to remove glycosylation sites of expressed proteins by modifying/altering nucleic acids encoding

the proteins for the purpose of optimized protein production in host cells of interest. (Withers-Martinez et al 1999, of record). In addition, the specific modification of nucleic acids encoding proteins of interest so as to utilize a host cell's codon usage (i.e. codon optimization) was known in the art. More specifically, codon optimization for expression of proteins of interest in yeast cells, and specifically for *P. falciparum* was described in Withers-Martinez et al (e.g. Abstract and Introduction, p. 1113).

However, the polynucleotide sequence of SEQ ID NO:6 is free of the prior art and due to the unpredictable nature of Applicants invention, it would not have been obvious at the time of Applicants invention to have explicitly used SEQ ID NO:6 in Applicants claimed method for producing mRNA and/or protein for preparation of a malaria vaccine.

Additionally, Lanar et al in *"Plasmodium Falciparum* AMA-1 Protein and Uses thereof" [USPGPub No. 2006/0264619A1, which claims priority to US Provisional Application 60/278,616, filed 26 March 2001] teaches a method for producing the ectodomain of the AMA-1 protein from the *P. falciparum* (3D7 strain) spanning amino acid residues 75-524 for use in eliciting antibodies in the field of malaria vaccines. While the US PGPub No. 2006/0264619A1 contemplates the use of modified AMA-1 sequence incorporating *E.coli* codon bias and suggests several host cell types including yeast cells (¶ 70), lines 1-4), these limitations are not contemplated in the US Provisional Application 60/278,616. Lanar et al fails to teach the nucleic acid structure of the instant application and 60/278,616 fails to teach expressing the P. *falciparum* AMA-

1 in yeast cells and fails to teach the use of yeast cell codon bias for optimization of the expression of yeast cell translation products as recited in the instant application.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CATHERINE S. HIBBERT whose telephone number is (571)270-3053. The examiner can normally be reached on M-F 8AM-5PM, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Respectfully submitted,

Catherine S. Hibbert
Examiner/AU1636

/ Christopher S. F. Low /
Supervisory Patent Examiner, Art Unit 1636